

REMARKS/ARGUMENTS

Claims 13-29 are pending in the captioned application. Claims 28-29 are withdrawn from consideration while claims 13-27 are finally rejected. Applicants respectfully request reconsideration and allowance of the claims.

In response to Applicants' amendment after Final, the Examiner states in the Advisory Action that the proposed amendment of claim 13 constitutes new matter and must be deleted. Applicants respectfully disagree.

Applicants submit that the proviso merely narrows the claim and does not constitute new matter. Basis for the amendment may be found in the patent application as filed, see for example:

- i) Figure 1, which provides the structure of the basic building block for the ET dyes of the present invention and shows preferred positions for attachment of other fluorophores including the sites both of R1 and X1 or X2.
- ii) Figure 2, which shows a bi-fluor ET dye with arrows showing possible attachment sites for further fluorophores including the R1 position.
- iii) Page 8, lines 5-7 which specifies that R1 includes -L2-D2.
- iv) Page 8, lines 12-16 which specifies that X1-X4 includes -L3-D3.
- v) Page 12, line 6 through page 13, line 11, which describes embodiments where ET dyes may include further fluorochromes.
- vi) The description at page 15 lines 6-25 which refers to energy transfer between two or more fluorophores linked together.
- vii) Also Example 4.2 (page 22-23) which shows the synthesis of a trifluor dye.

Consequently, Applicants submit that the Examiner's new matter rejection in the Advisory Action is not understood. Applicants believe that the new matter rejection is improper since the proviso of claim 13 is fully supported by the application as filed. Applicants submit that the new matter rejection should be withdrawn.

In response to Applicants' amendment after Final, the Examiner again regards the claims as being obvious over the cited prior art (Lee et al., US 5863727, in view of Burdette et al., J. Amer. Chem. Soc., (2001), 123, 7831-41). Applicants respectfully disagree.

Applicants first submit that claim 13, as amended, relates to a compound which is a tri-fluor energy transfer (ET) dye.

Applicants submit that Lee et al. describes energy transfer dyes having a fluorescent donor dye which absorbs light at a first wavelength and a fluorescent acceptor dye which is capable of absorbing the excitation energy emitted by the donor dye and fluorescing at a second wavelength. None of the examples in Lee et al. specifically disclose a tri-fluor ET dye. There appears to be no mention of a cascade of ET events that would be associated with more than two fluorochromes in an energy transfer relationship.

Applicants also submit that Burdette et al. describes two fluorescent sensors for detecting zinc. Particular examples are shown on page 7835 (Compound 5) and page 7836 (Compound 4). Both examples show a single fluorophore (having the fluorescein structure) having 2-pyridylmethyl amino groups attached through the 4' and 5' positions. These positions are equivalent to the R11 and R14 positions shown in Lee et al. The pyridylmethyl substituents serve to coordinate the zinc ion. See scheme 3, page 7839. The zinc sensors described by Burdette et al. are not ET dyes.

The Examiner alleges, on page 2 of the Office action dated August 27, 2007, that Burdette et al. teaches fluorescent dyes that are similar to the instantly claimed dyes. Applicants contend that this statement is not correct because Burdette et al. does not teach energy transfer dyes, merely a single dye derivative that is capable of coordinating zinc ions. Energy transfer does not take place - only an increase in fluorescence of the fluorescein, upon coordination of the zinc ions. Applicants contend therefore that the instant invention is not *prima facie* obvious from the teachings, as Burdette et al. adds nothing to cure the deficiency of Lee et al.

The Examiner alleges (page 3) that "One of ordinary skill in the art would have known to claim dyes wherein R11 and R14 are amine at the same time as Y1 is OH and Y2 is oxygen from the generic teaching of Lee." It should be pointed out that the present invention does not claim R11- and R14-amino derivatives. Whilst from Figure 1 of the present application, it can be seen that the functional groups in

these positions are aminomethyl (i.e., the amino group is not directly attached to the fluorescein chromophore), the claims under examination relate to tri-fluor ET dyes and not just to bis-aminomethyl derivatives of a single fluorophore.

Furthermore, whether or not Burdette et al. discloses tertiary amines as an obvious variant of a secondary amine (as stated by the Examiner, page 3) is considered by Applicants to be irrelevant because Burdette et al. lacks any teaching *a priori* about ET dyes, and more particularly about tri-fluor ET dyes.

Applicants also contend that Burdette et al. provides no motivation to use R11- and R14-amino derivatized fluorescein as a starting point for further modifications. This is because the reference states that "The ability to modify synthetically commercially available substituted fluorescein compounds such as fluorescein amine is often limited because the compounds are relatively unreactive and require harsh conditions." (page 7840, column 2, Conclusions). This is a disincentive to the skilled person to consider Burdette et al. as a useful starting point for completing the information missing from Lee et al.

The Examiner has stated (page 3) that Burdette et al. provides the road (i.e. the route) leading to the trees. Applicants presume that this statement is intended to mean that Burdette et al. provides guidance to enable the teachings of Lee et al. to be modified. By contrast, in view of the above discussion, Applicants contend

that Burdette et al. provides neither the motivation nor the teaching to enable a skilled person to modify the teachings of Lee et al. in order to arrive at the present claims.

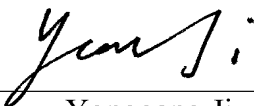
Claim 13 as presently amended is considered to be non-obvious over Lee et al. in view of Burdette et al.

Applicants respectfully assert that the claims are in allowable form and earnestly solicit the allowance of pending claims.

Early and favorable consideration is respectfully requested.

Respectfully submitted,

GE Healthcare Bio-Sciences Corp.

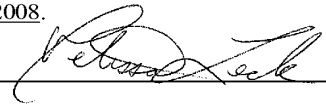
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